
Chemical Mixture

No CAS #

Sprague-Dawley rats, at 10, 50, and 100X

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Environmental Health Research and Testing

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This mixture*, a cocktail of 25 organic compounds and metals found in contaminated groundwater supplies, was tested as part of a larger program to evaluate a variety of possible effects of such a mixture in several species [Yang et al., *Fundam Appl Toxicol* 13:366–376 (1989); Chapin et al., *Fundam Appl Toxicol* 13:388–398 (1989)]. This reproductive toxicity study used Sprague-Dawley rats in the RACB protocol (Heindel et al., *Fundam Appl Toxicol* 25:9–19 [1995]). Doses of 10, 50, and 100X in water were selected, based on previous National Toxicology Program data. (A standard solution, designated “1000X”, contained the greatest possible concentration of all 25 chemicals in the mix. The dose levels represent 0, 1, 5, and 10% of this “1000X” level, or “0, 10, 50, and 100X levels”). The concentrations of each component of the mixture are specified in Tables 1–3 of the final technical report.

No adverse clinical signs were noted during Task 2, although water consumption was reduced by 10, 30, and 40% in the low to high dose groups, respectively.

Related to these reductions, body weights for high dose F₀ males and females were reduced but were never more than 10% less than control values.

Reproductive effects were limited to a 6% reduction in adjusted live pup weight at the high dose, and a 10 and 15% reduction in the number of live male pups at the low and high dose levels, respectively. This correlated with 9% fewer live pups per litter at the low dose. The middle dose level was unaffected.

In the absence of statistical evaluation, these effects were considered minor, and no Task 3 crossover evaluation was performed.

The last litter was nursed to weaning. Pup weights during this period were reduced in the middle and high dose groups by approximately 14 and 30%, respectively. Female pup mortality was increased at the high dose (≈20% fewer treated pups than controls survived to weaning).

Subsequent evaluation of this generation continued for high dose and control animals only. At mating, treated females weighed approximately 15% less than controls.

Litters of F₂ pups were of equal size and viability, but litters from the treated dams were approximately 15% lighter than controls.

After the F₂ pups were delivered and evaluated, the F₁ adults were killed and necropsied. For treated males, terminal body weight was reduced by approximately 16% while relative kidney weights increased by 15%. Absolute testis weight decreased by approximately 9%, while relative epididymal and seminal vesicle weights increased by 10 and 15% respectively; sperm measures were unchanged by consumption of the mixture. For treated females, body weight was reduced by approximately 12%, while adjusted kidney weight was increased by approximately 15%. Antemortem estrous cycle length and proportions were the same in both groups.

In conclusion, exposure of Sprague-Dawley rats to this mixture produced mild reproductive effects (slight reductions in adjusted pup weight and number of male pups) in the presence of significant decreases in fluid consumption, and increased relative kidney weight.

*Chemical Mixture (concentrations in ppm for 100X group): acetone (53), Arochlor 1260 (0.01), arsenic (9), benzene (12.5), cadmium (51), carbon tetrachloride (0.4), chlorobenzene (0.1), chloroform (7), chromium (36), di(2-ethylhexyl)phthalate (0.015), 1,1-dichloroethane (1.4), 1,2-dichloroethane (40), 1,1-dichloroethylene (0.5), 1,2-trans-dichloroethylene (2.5), ethylbenzene (0.3), lead (70), mercury (0.5), methylene chloride (37.5), nickel (6.8), phenol (29), tetrachloroethylene (3.4), toluene (7), 1,1,1-trichloroethane (2), trichloroethylene (6.5), xylenes (1.6).

CHEMICAL MIXTURE

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: 91184739

Chemical: Chemical Mixture

CAS#: None

Mode of exposure: Water

Species/strain: SD rats

F ₀ generation	Dose concentration →	10X	50X	100X
General toxicity		Male, female	Male, female	Male, female
Body weight		—, —	—, —	↓, —
Kidney weight ^a		•, •	•, •	•, •
Liver weight ^a		•, •	•, •	•, •
Mortality		—, —	—, —	—, —
Feed consumption		•, •	•, •	•, •
Water consumption		↓, ↓	↓, ↓	↓, ↓
Clinical signs		—, —	—, —	—, —

Reproductive toxicity			
̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	↓, —	—, —	—, ↓
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight ^a	•, •	•, •	—, •
Sex accessory gland weight ^a (prostate, seminal vesicle)	•, •	•, •	•, •
Epidid. sperm parameters (#, motility, morphology)	•, •, •	•, •, •	•, •, •
Estrous cycle length	•	•	•

Determination of affected sex (crossover)	Male	Female	Both
Dose level	•	•	•

F ₁ generation	Dose concentration →	10X	50X	100X
General toxicity		Male, female	Male, female	Male, female
Pup growth to weaning		—, —	↓, ↓	↓, ↓
Mortality		—, —	—, —	—, ↑
Adult body weight		•, •	•, •	↓, ↓
Kidney weight ^a		•, •	•, •	↑, ↑
Liver weight ^a		•, •	•, •	—, —
Feed consumption		•, •	•, •	•, •
Water consumption		•, •	•, •	↓, ↓
Clinical signs		•, •	•, •	—, —

Reproductive toxicity			
Fertility index	•, •	•, •	—
# live pups/litter; pup wt./litter	•, •	•, •	—, ↓
Absolute testis, epididymis weight ^a	•, •	•, •	↓, ↑
Sex accessory gland weight ^a (prostate, seminal vesicle)	•, •	•, •	—, ↑
Epidid. sperm parameters (#, motility, morphology)	•, •, •	•, •, •	—, —, —
Estrous cycle length	•	•	—

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	<10X
NOAEL general toxicity:	10X
F ₁ more sensitive than F ₀ ?	No
Postnatal toxicity:	Yes

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. ^aAdjusted for body weight.